



427.045-DIV-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
BIGG et al
Serial No.:
Filed: Concurrently Herewith
For: NEW...CONTAINING THEM

Examiner: S. Patel
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New York, NY 10016

PRELIMINARY AMENDMENT

Hon. Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Please amend this application as follows:

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks begin on page 9 of this paper.

shrpS

*M. Chet W.
Knechtel et al
XII/07/06
it's toxic*

New derivatives of N-(iminomethyl)amines, their preparation, their use as medicaments and the pharmaceutical compositions containing them

--This application is a division of U.S. patent application Serial No. 09/787,466 filed March 16, 2001, now U.S. Patent No. 6482822 which is a 371 of PCT/FR99/02251 filed September 22, 1999.--

A subject of the present invention is new derivatives of N-(iminomethyl)amines comprising the aminodiphenylamine, oxodiphenylamine, carbazole, phenazine, phenothiazine, phenoxazine or oxodiphenyl unit in their skeleton. These derivatives have an inhibitory activity on NO-synthase enzymes producing nitrogen monoxide NO and/or an activity which traps the reactive oxygen species (ROS). The invention relates to the derivatives corresponding to general formula (I) defined below, their preparation methods, the pharmaceutical preparations containing them and their use for therapeutic purposes, in particular their use as NO-synthase inhibitors and selective or non selective traps for reactive oxygen species.

- 10 Given the potential role of NO and the ROS's in physiopathology, the new derivatives described corresponding to general formula (I) may produce beneficial or favourable effects in the treatment of pathologies where these chemical species are involved. In particular:
 - Proliferative and inflammatory diseases such as for example atherosclerosis, pulmonary hypertension, respiratory distress, glomerulonephritis, portal hypertension, psoriasis, arthrosis and rheumatoid arthritis, fibroses, angiogenesis, amyloidoses, inflammations of the gastro-intestinal system (ulcerous or non-ulcerous colitis, Crohn's disease), diarrhoea.
 - Diseases affecting the pulmonary system and airways (asthma, sinusitis, rhinitis).
- 15 20 Cardio-vascular and cerebro-vascular disorders including for example, migraine, arterial hypertension, septic shock, ischemic or hemorrhagic, cardiac or cerebral infarctions, ischemias and thromboses.